



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 109084

TO: Gina C Yu
Location: cm1/3c01/2b19
Art Unit: 1617
Sunday, November 30, 2003

Case Serial Number: 10/070601

From: Mary Jane Ruhl
Location: Biotech-Chem Library
CM1-6A06
Phone: 605-1155

maryjane.ruhl@uspto.gov

Search Notes

Examiner Yu,

Here are the results for your recent search request.

Please feel free to contact me if you have any questions about these results.

Thank you for using STIC services. We appreciate the opportunity to serve you.

Sincerely,

Mary Jane Ruhl
Technical Information Specialist
STIC
CM-1, Rm. 6-A-06
605-1155

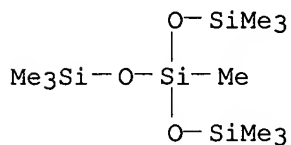
This is the requested compound.

Yu 10/070,601

30/11/2003

=> d 17

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 17928-28-8 REGISTRY
CN Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-(trimethylsiloxy)- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 1,1,1,3,5,5,5-Heptamethyl-3-(trimethylsiloxy)trisiloxane
CN Methyltris(trimethylsiloxy)silane
CN Tris(trimethylsiloxy)methylsilane
MF C10 H30 O3 Si4
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHM, DETHERM*, GMELIN*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

81 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
81 REFERENCES IN FILE CAPLUS (1907 TO DATE)
16 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d que stat 18

L7 1 SEA FILE=REGISTRY ABB=ON 17928-28-8/RN
 L8 5 SEA FILE=HCAPLUS ABB=ON (L7 OR M3T) AND (?DERM? ?SKIN? OR
 ?CUTAN? OR ?PHARM? OR ?COSMET? OR ?PERSON?(W)?CARE?)

=> => d ibib abs hitstr hitrn 18 1-5

L8 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:714163 HCAPLUS

DOCUMENT NUMBER: 137:232767

TITLE: Preparation of branched siloxanes useful as industrial
 siloxane lubricants, **cosmetic** fluids, and
 cleaning agents.

INVENTOR(S): Asai, Satoshi; Tsukioka, Kazumasa

PATENT ASSIGNEE(S): Shin-Etsu Chemical Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 7 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1241171	A1	20020918	EP 2002-251818	20020314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002265478	A2	20020918	JP 2001-71788	20010314
US 2002133035	A1	20020919	US 2002-96589	20020314
US 6596892	B2	20030722		

PRIORITY APPLN. INFO.: JP 2001-71788 A 20010314

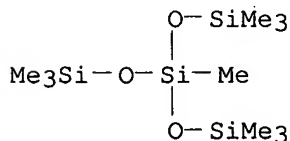
OTHER SOURCE(S): CASREACT 137:232767

AB Branched siloxanes, [e.g., methyltris(trimethylsiloxy)silane] are
 effectively prepared in high yields by reacting a trichlorosilane (e.g,
 methyltrichlorosilane) with a disiloxane (e.g., hexamethyldisiloxane) in
 the presence of a linear phosphonitric chloride (LPNC) catalyst.
 Comps. of the type prepared are useful as industrial siloxane lubricants,
cosmetic fluids, and cleaning agents.

IT 17928-28-8P, Methyltris(trimethylsiloxy)silane
 RL: IMF (Industrial manufacture); PREP (Preparation)
 (preparation of branched siloxanes)

RN 17928-28-8 HCAPLUS

CN Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]- (9CI) (CA
 INDEX NAME)



IT 17928-28-8P, Methyltris(trimethylsiloxy)silane
 RL: IMF (Industrial manufacture); PREP (Preparation)
 (preparation of branched siloxanes)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:169510 HCAPLUS
 DOCUMENT NUMBER: 136:205209
 TITLE: Oily **cosmetic** compositions containing
 branched volatile organopolysiloxanes
 INVENTOR(S): Kuroda, Akihiro; Egawa, Yuichiro
 PATENT ASSIGNEE(S): Kanebo, Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002068930	A2	20020308	JP 2000-258501	20000829

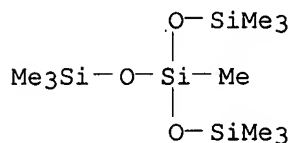
PRIORITY APPLN. INFO.: JP 2000-258501 20000829

AB The invention relates to an oily **cosmetic** composition, especially a lipstick composition, providing improved use feel and prolonged makeup effect, wherein the composition contains a branched volatile organopolysiloxane (Me₃SiO)₃SiMe. A compound (Me₃SiO)₃SiMe was prepared from trimethylchlorosilane and methyltrichlorosilane and combined at 40 % with trimethylsiloxysilicic acid 5, ceresin 15, castor oil 18, red 202 1, titanium oxide 1, mica titanium 20 % to obtain a lipstick composition

IT **17928-28-8P**
 RL: COS (Cosmetic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (oily **cosmetic** compns. containing branched volatile organopolysiloxanes and other ingredients)

RN 17928-28-8 HCAPLUS

CN Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]- (9CI) (CA INDEX NAME)

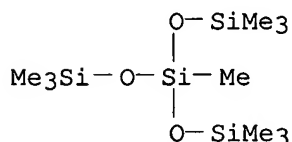


IT **17928-28-8P**
 RL: COS (Cosmetic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (oily **cosmetic** compns. containing branched volatile organopolysiloxanes and other ingredients)

L8 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:167776 HCAPLUS
 DOCUMENT NUMBER: 134:212507
 TITLE: **Cosmetics** containing branched volatile organopolysiloxanes
 INVENTOR(S): Kuroda, Akihiro; Sakuta, Koji; Usui, Hitoshi
 PATENT ASSIGNEE(S): Kanebo, Ltd., Japan; Shin-Etsu Chemical Co., Ltd.
 SOURCE: PCT Int. Appl., 82 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015658	A1	20010308	WO 2000-JP5838	20000829
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1213006 A1 20020612 EP 2000-955104 20000829 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL PRIORITY APPLN. INFO.: JP 1999-242948 A 19990830 JP 1999-242949 A 19990830 JP 1999-266824 A 19990921 WO 2000-JP5838 W 20000829				
AB	Cosmetics characterized by containing an organopolysiloxane (Me ₃ SiO)SiMe (I). The cosmetics exhibit excellent volatility and feels and are excellent in stability. A compound I was prepared by hydrolysis of a mixture of trimethylchlorosilane and Me trichlorosilane, and combined at 25 % with silicone-treated TiO ₂ particles 3, polyoxyethylene-methylpolysiloxane copolymer (KF6017) 1, silicone-treated. zinc oxide particle 6, perfluoroalkylphosphate-treated mica 0.5, crosslinked organopolysiloxane spherical powders 4, dimethylpolysiloxane (KF96A-6) 2, fluorinated dimethiconol 1, trimethylsiloxysilicate solution 6, octyl-p-methoxysilicate 3, p-fluoropolyether 0.5, ethanol 10, ale extract 1, hamamelis extract 1, hibiscus extract 0.5, and water q.s. to 100 % to obtain a sunscreen makeup base.			
IT	17928-28-8P RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)			
RN	17928-28-8 HCAPLUS			
CN	Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]- (9CI) (CA INDEX NAME)			



IT **17928-28-8P**
 RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**cosmetics** containing branched volatile organopolysiloxanes and other polysiloxanes)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1993:595083 HCAPLUS
 DOCUMENT NUMBER: 119:195083

TITLE: Metabolism and pharmacokinetics of the anti-HIV-1-specific inhibitor [1-[2',5'-bis-O-(tert-butyldimethylsilyl)- β -D-ribofuranosyl]-3-N-methylthymine]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide)

AUTHOR(S): Balzarini, Jan; Naesens, Lieve; Bohman, Christina; Perez-Perez, Maria Jesus; San-Felix, Ana; Camarasa, Maria Jose; De Clerco, Erik

CORPORATE SOURCE: Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.

SOURCE: Biochemical Pharmacology (1993), 46(1), 69-77
CODEN: BCPA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB [1-[2',5'-Bis-O-(tert-butyldimethylsilyl)- β -D-ribofuranosyl]-3-N-methylthymine]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide) (TSAO-m3T) is a potent, selective and specific inhibitor of human immunodeficiency virus type 1 replication in vitro. Uptake of TSAO-m3T by the human T4 lymphocyte CEM cells is drug concentration-dependent and increased proportionally with increasing initial extracellular TSAO-m3T concns. up to 20 μ g/mL. Within 6 h of incubation, the cells were almost completely saturated with the test compound; further incubation up to 72 h did not markedly increase the intracellular concentration of the compound. No intracellular metabolic conversion of TSAO-m3T was observed in CEM, MT-4 or MOLT-4 cells. Upon i.v. bolus administration of TSAO-m3T to mice at 0.75 mg/kg, TSAO-m3T was rapidly cleared from the plasma in a mono-exponential manner (half-life: 2 min; distribution volume: 9.5 L/kg; total body clearance: 17.8 L/h/kg). TSAO-m3T mainly accumulated in the lungs, followed by the heart, kidney and liver. Significant amts. of different metabolites of TSAO-m3T were detected in most tissues, the liver, kidney and spleen being the organs that showed the most extensive metabolism. The principal metabolites identified were TSAO-m3T derivs. in which the t-butyldimethylsilyl moiety at C-2' and/or C-5' had been split off. The free base N3-methylthymine was not detected.

L8. ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1991:128802 HCAPLUS

DOCUMENT NUMBER: 114:128802

TITLE: Cosmetic composition containing siloxanes and saturated hydrocarbon oils

INVENTOR(S): Sakuta, Koji; Kuwata, Satoshi

PATENT ASSIGNEE(S): Shin-Etsu Chemical Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

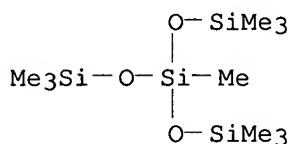
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 383540	A2	19900822	EP 1990-301507	19900213
EP 383540	A3	19910911		
EP 383540	B1	19950503		
R: DE, FR, GB				
JP 02214775	A2	19900827	JP 1989-35836	19890215
JP 06060286	B4	19940810		
US 4970252	A	19901113	US 1990-480004	19900214
PRIORITY APPLN. INFO.:			JP 1989-35836	19890215

- AB An oily paste composition comprises (1) a polymerization product obtained by addition polymerization of (a) an organohydrogensiloxane containing ≥ 1.5 Si-bonded H on average and (b) an organosiloxane containing ≥ 1.5 Si-bonded aliphatic unsatd. group on average and (2) a saturated hydrocarbon oil. The composition which is smooth to touch, free from stickiness and transparent is used for **cosmetic** or medical purposes. Trimethylsilyl-terminated dimethylhydrogensiloxane and dimethylvinylsilyl-terminated dimethylsiloxane and dimethylsiloxane were mixed and a solution of chloroplatinate in iso-PrOH was added. The mixture was heated at 70-80° for 2 h to obtain a soft polymer powder. The polymer powder was mixed with Isopar G (C9-12 isoalkane) and kneaded in a 3-roll mill to obtain an oily paste which was transparent and had a viscosity of 17,000 cP as compared to 2,000 for the control which had no dimethylsiloxane and was cloudy.
- IT 17928-28-8D, Methyltris(trimethylsiloxy)silane, reaction products
RL: BIOL (Biological study)
(**cosmetic** composition containing saturated hydrocarbon oil and)
- RN 17928-28-8 HCAPLUS
- CN Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]- (9CI) (CA INDEX NAME)



- IT 17928-28-8D, Methyltris(trimethylsiloxy)silane, reaction products
RL: BIOL (Biological study)
(**cosmetic** composition containing saturated hydrocarbon oil and)

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L7 1 SEA FILE=REGISTRY ABB=ON 17928-28-8/RN
L8 5 SEA FILE=HCAPLUS ABB=ON (L7 OR M3T) AND (?DERM? ?SKIN? OR
?CUTAN? OR ?PHARM? OR ?COSMET? OR ?PERSON?(W)?CARE?)
L9 19 SEA L8
L10 14 DUP REMOV L9 (5 DUPLICATES REMOVED)

=> d ibib abs 110 1-14

L10 ANSWER 1 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:340728 BIOSIS

DOCUMENT NUMBER: PREV200100340728

TITLE: Identification of a putative binding site for
(2',5'-bis-O-(tert-butyldimethylsilyl)-beta-D-
ribofuranosyl)-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-
2'',2''-dioxide)thymine (TSAO) derivatives at the p51-p66
interface of HIV-1 reverse transcriptase.

AUTHOR(S): Rodriguez-Barrios, Fatima; Perez, Carlos; Lobaton, Esther;
Velazquez, Sonsoles; Chamorro, Cristina; San-Felix, Ana;
Perez-Perez, Maria-Jesus; Camarasa, Maria-Jose; Pelemans,
Heidi; Balzarini, Jan; Gago, Federico [Reprint author]

CORPORATE SOURCE: Departamento de Farmacologia, Universidad de Alcala,
E-28871, Alcala de Henares, Madrid, Spain
federico.gago@uah.es

SOURCE: Journal of Medicinal Chemistry, (June 7, 2001) Vol. 44, No.
12, pp. 1853-1865. print.
CODEN: JMCMAR. ISSN: 0022-2623.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 18 Jul 2001

Last Updated on STN: 19 Feb 2002

AB A binding site for TSAO-m3T at the interface between the p66 and
p51 subunits of HIV-1 reverse transcriptase (RT) and distinct from that of
"classical" HIV-1 non-nucleoside inhibitors is proposed. The feasibility
of the binding mode was assessed by carrying out nanosecond molecular
dynamics simulations for the complexes of TSAO-m3T with reduced
models of both the wild-type enzyme and a more sensitive R172A mutant.
The molecular model is in agreement with a previous proposal, with known
structure-activity and mutagenesis data for this unique class of
inhibitors, and also with recent biochemical evidence indicating that TSAO
analogues can affect enzyme dimerization. The relative importance of
residues involved in dimer formation and TSAO-RT complex stabilization was
assessed by a combination of surface area accessibility, molecular
mechanics, and continuum electrostatics calculations. A structure-based
modification introduced into the lead compound yielded a new derivative
with improved antiviral activity.

L10 ANSWER 2 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1999:381747 BIOSIS

DOCUMENT NUMBER: PREV199900381747

TITLE: Unexpected results in the reaction of 5'-tosyl TSAO-
m3T with amines.

AUTHOR(S): Chamorro, C. [Reprint author]; Velazquez, S. [Reprint
author]; Jimeno, M. L. [Reprint author]; Perez-Perez, M. J.
[Reprint author]; Lobaton, E. [Reprint author]; Tunon, V.
[Reprint author]; Esteban-Gamboa, A. [Reprint author];
Gago, F.; De Clercq, E.; Balzarini, J.; Camarasa, M. J.
[Reprint author]; San-Felix, A. [Reprint author]

CORPORATE SOURCE: Instituto de Quimica Medica (C.S.I.C.), Madrid, Spain
SOURCE: Nucleosides and Nucleotides, (April-May, 1999) Vol. 18, No.

4-5, pp. 715-716. print.
CODEN: NUNUD5. ISSN: 0732-8311.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 1999
Last Updated on STN: 13 Sep 1999

AB We report our strategies to prepare TSAO compounds carrying at 5'-position groups, such as amines, that may be positively charged at physiological conditions, unexpectedly, cyclic TSAO-derivatives were obtained. A possible mechanism for the formation of these unexpected compounds is advanced.

L10 ANSWER 3 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 1998268175 EMBASE
TITLE: Novel 3'-spiro nucleoside analogues of TSAO-T. Part II. A comparative study based on NMR conformational analysis in solution and theoretical calculations.
AUTHOR: Alvarez R.; Jimeno M.-L.; Gago F.; Balzarini J.;
Perez-Perez M.-J.; Camarasa M.-J.
CORPORATE SOURCE: M.-J. Camarasa, Instituto de Quimica Medica, CSIC, Juan de la Cierva 3, 28006 Madrid, Spain. mariajose@pinarl.csic.es
SOURCE: Antiviral Chemistry and Chemotherapy, (1998) 9/4 (333-340).
Refs: 36
ISSN: 0956-3202 CODEN: ACCHEH
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English

AB The structures of two novel 3'-spiro nucleosides analogues of the potent human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT) inhibitor TSAO-m3T, in solution, as derived from NMR spectroscopy are described. In these TSAO analogues the spiro amino oxathioledioxide moiety has been replaced by spiro amino oxazolone or spiro amino oxathiazoledioxide moieties. A comparative study based on theoretical calculations of the hydrophobicity, the solvation free energies and molecular electrostatic potentials (MEP) of the three compounds is also described. No significant conformational differences were detected in solution between TSAO-m3T and its analogues that might account for the differences observed in their inhibitory activity against HIV-1 RT. The calculated hydrophobicity (log P) values, dipole moments and the electrostatic contributions to the solvation free energies of the three spiro ring systems were also similar. However, the differences found in the calculated MEPs of the spiro systems between TSAO-m3T and its analogues suggest that the different electrostatic surroundings of the 4'-amino group of the spiro moiety in the analogues may be responsible for a detrimental electrostatic interaction of the spiro rings with the Glu- B138 of RT.

L10 ANSWER 4 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:44204 BIOSIS
DOCUMENT NUMBER: PREV199800044204
TITLE: Synthesis and anti-human immunodeficiency virus type 1 activity of novel 3'-spiro nucleoside analogues of TSAO-T.
AUTHOR(S): Alvarez, R.; Jimeno, M.-L.; Perez-Perez, M.-J.; De Clercq, E.; Balzarini, J.; Camarasa, M.-J. [Reprint author]
CORPORATE SOURCE: Inst. Quim. Med., CSIC, Juan de la Cierva 3, 28006 Madrid,

SOURCE: Spain
Antiviral Chemistry and Chemotherapy, (Nov., 1997) Vol. 8,
No. 6, pp. 507-517. print.
CODEN: ACCHEH. ISSN: 0956-3202.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jan 1998
Last Updated on STN: 27 Jan 1998

AB Novel 3'-spiro nucleoside analogues of the potent human immunodeficiency virus type I (HIV-1) reverse transcriptase (RT) inhibitor TSAO-T have been designed, synthesized and tested for their in vitro antiretroviral activity against HIV-1. In these TSAO analogues the spiro amino-oxathioledioxide moiety was replaced by other spiro moieties that maintained an NH group at the same position as the 4"-NH₂ group in the prototype compound TSAO-T. Anti-HIV-1 activity, although around 100-fold less pronounced than that of the parent TSAO-m₃T derivative, was observed for the spiro oxazolone derivative. The spiro oxathiazoledioxide compound also showed antiviral activity. The corresponding beta-D-xylofuranosyl analogues were devoid of antiviral activity; this is in accordance with the behaviour of TSAO-m₃T. None of the test compounds were inhibitory to HIV-2 replication. The markedly decreased potency of the spiro oxathiazoledioxide and oxazolone compounds against HIV-1 replication is in agreement with their decreased anti-HIV-1 RT activity.

L10 ANSWER 5 OF 14 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 97051861 MEDLINE
DOCUMENT NUMBER: 97051861 PubMed ID: 8896496
TITLE: Multiple drug resistance to nucleoside analogues and nonnucleoside reverse transcriptase inhibitors in an efficiently replicating human immunodeficiency virus type 1 patient strain.
AUTHOR: Schmit J C; Cogniaux J; Hermans P; Van Vaeck C; Sprecher S; Van Remoortel B; Witvrouw M; Balzarini J; Desmyter J; De Clercq E; Vandamme A M
CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Belgium.
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1996 Nov) 174 (5) 962-8. Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
OTHER SOURCE: GENBANK-AJ002370; GENBANK-AJ002371; GENBANK-AJ002372; GENBANK-AJ002373; GENBANK-AJ002374; GENBANK-AJ002375; GENBANK-AJ002376
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 20000303
Entered Medline: 19961127

AB A human immunodeficiency virus type 1 (HIV-1)-seropositive patient was treated sequentially with the dideoxynucleoside (ddN) analogues zidovudine, didanosine, zalcitabine, stavudine, and lamivudine and the nonnucleoside HIV-1-specific reverse transcriptase inhibitor (NNRTI) loviride (alpha-APA). Accumulation of drug resistance mutations (mainly V75I, F77L, K103N, F116Y, Q151M, and M184V) eventually resulted in a strain that was genotypically and phenotypically resistant to all tested ddNs and the majority of NNRTIs. However, the multidrug-resistant virus retained wild type sensitivities to drugs such as foscarnet, phosphonomethoxyethyl adenine, dextran sulfate, JM3100, saquinavir, and

NNRTI TSAO-m3T. Drug-resistant isolates showed replication kinetics and infectivity in an in vitro peripheral blood mononuclear cell system similar to those of the wild type isolate from the same patient. The multi-ddN-resistant isolate was not eliminated in a competition culture with the wild type isolate. Sequential therapy did not prevent the appearance of multidrug-resistant virus with a conserved replication rate.

L10 ANSWER 6 OF 14 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 95296332 MEDLINE
 DOCUMENT NUMBER: 95296332 PubMed ID: 7539917
 TITLE: Suppression of the breakthrough of human immunodeficiency virus type 1 (HIV-1) in cell culture by thiocarboxanilide derivatives when used individually or in combination with other HIV-1-specific inhibitors (i.e., TSAO derivatives).
 AUTHOR: Balzarini J; Perez-Perez M J; Velazquez S; San-Felix A; Camarasa M J; De Clercq E; Karlsson A
 CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Belgium.
 SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Jun 6) 92 (12) 5470-4. Journal code: 7505876. ISSN: 0027-8424.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; AIDS
 ENTRY MONTH: 199507
 ENTRY DATE: Entered STN: 19950720
 Last Updated on STN: 19980206
 Entered Medline: 19950712

AB Five structurally related thiophene and furane analogues of the oxathiin carboxanilide derivative NSC 615985 (UC84) (designated UC10, UC68, UC81, UC42, and UC16) were identified as potent inhibitors of HIV-1 replication in cell culture and HIV-1 reverse transcriptase activity. These compounds were markedly active against a series of mutant HIV-1 strains, containing the Leu-100-->Ile, Val-106-->Ala, Glu-138-->Lys, or Tyr-181-->Cys mutations in their reverse transcriptase. However, the thiocarboxanilide derivatives selected for mutations at amino acid positions 100 (Leu-->Ile), 101 (Lys-->Ile/Glu), 103 (Lys-->Thr/Asp) and 141 (Gly-->Glu) in the HIV-1 reverse transcriptase. The compounds completely suppressed HIV-1 replication and prevented the emergence of resistant virus strains when used at 1.3-6.6 microM--that is, 10- to 25-fold lower than the concentration required for nevirapine and bis(heteroaryl)piperazine (BHAP) U90152 to do so. If UC42 was combined with the [2',5'-bis-O-(tert-butyl)dimethylsilyl]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide)]-beta-D-pentofuranosyl (TSAO) derivative of N3-methylthymine (TSAO-m3T), virus breakthrough could be prevented for a much longer time, and at much lower concentrations, than if the compounds were used individually. Virus breakthrough could be suppressed for even longer, and at lower drug concentrations, if BHAP was added to the combination of UC42 with TSAO-m3T, which points to the feasibility of two- or three-drug combinations in preventing virus breakthrough and resistance development.

L10 ANSWER 7 OF 14 MEDLINE on STN
 ACCESSION NUMBER: 95321948 MEDLINE
 DOCUMENT NUMBER: 95321948 PubMed ID: 7541200
 TITLE: Sensitivity/resistance profile of a simian immunodeficiency virus containing the reverse transcriptase gene of human immunodeficiency virus type 1 (HIV-1) toward the

HIV-1-specific non-nucleoside reverse transcriptase inhibitors.

AUTHOR: Balzarini J; Weeger M; Camarasa M J; De Clercq E; Uberla K
 CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke
 Universiteit Leuven, Belgium.
 SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995
 Jun 26) 211 (3) 850-6.
 Journal code: 0372516. ISSN: 0006-291X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; AIDS
 ENTRY MONTH: 199508
 ENTRY DATE: Entered STN: 19950817
 Last Updated on STN: 19960129
 Entered Medline: 19950801

AB To develop an animal model for the therapy of AIDS with human immunodeficiency virus type 1 (HIV-1)-specific reverse transcriptase (RT) inhibitors, we recently constructed a hybrid simian immunodeficiency virus (SIV)/HIV-1 in which the RT gene of SIV was replaced by the RT gene of HIV-1. This chimaeric virus, designated RT-SHIV, was found to be markedly sensitive to the inhibitory effects of both nucleoside (ddN) and non-nucleoside RT inhibitors (NNRTIs). In contrast, SIV was inhibited only by ddNs (i.e., 3TC and AZT), but not NNRTIs. When RT-SHIV was grown in the presence of 3TC, nevirapine, TSAO-m3T or the thiocarboxanilide UC-42 drug-resistant mutant virus strains emerged in cell culture as rapid as for HIV-1(IIIB). The antiviral sensitivity/resistance spectrum of the mutant RT-SHIV strains against NNRTIs and ddNs, and the nature of the mutations that appeared in their RT were similar to those of the mutant HIV-1 strains that were selected under identical experimental conditions. Infection of macaques with RT-SHIV may be a useful tool for studying the mechanism of NNRTI-resistance development and the therapy of NNRTI-resistant viruses in an animal model.

L10 ANSWER 8 OF 14 MEDLINE on STN DUPLICATE 3
 ACCESSION NUMBER: 96145337 MEDLINE
 DOCUMENT NUMBER: 96145337 PubMed ID: 8540750
 TITLE: Synthesis and anti-HIV-1 activity of novel TSAO-T
 derivatives modified at the 2'- and 5'-positions of the
 sugar moiety.
 AUTHOR: Ingate S; Perez-Perez M J; De Clercq E; Balzarini J;
 Camarasa M J
 CORPORATE SOURCE: Instituto de Quimica Medica (C.S.I.C.), Madrid, Spain.
 SOURCE: ANTIVIRAL RESEARCH, (1995 Jun) 27 (3) 281-99.
 Journal code: 8109699. ISSN: 0166-3542.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; AIDS
 ENTRY MONTH: 199602
 ENTRY DATE: Entered STN: 19960221
 Last Updated on STN: 19970203
 Entered Medline: 19960206

AB Novel analogues of the anti-HIV-1 agent TSAO-T, [1-[2',5'-bis-O-(tert-butyl)dimethylsilyl)-beta-D-ribofuranosyl]thymine]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide) and its 3-methyl counterpart TSAO-m3T were obtained by modifications at positions 2' or 5' of the sugar moiety. These compounds were evaluated for their inhibitory effect on HIV-1 and HIV-2 replication in cell culture. Introduction of new groups at the 5'-position (i.e. esters, benzylether and silylethers)

resulted in compounds that were either inactive or less active than the parent compounds (TSAO-T and TSAO-m3T). Attempts to introduce small silyl ether groups at this position were not successful since these products decomposed during purification. Similar modifications at the 2'-position had a much less pronounced influence on the anti-HIV-1 activity.

L10 ANSWER 9 OF 14 MEDLINE on STN
 ACCESSION NUMBER: 95014312 MEDLINE
 DOCUMENT NUMBER: 95014312 PubMed ID: 7523383
 TITLE: Resistance of HIV-1 reverse transcriptase against [2',5'-bis-O-(tert-butyldimethylsilyl)-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide)] (TSAO) derivatives is determined by the mutation Glu138-->Lys on the p51 subunit.
 AUTHOR: Jonckheere H; Taymans J M; Balzarini J; Velazquez S; Camarasa M J; Desmyter J; De Clercq E; Anne J
 CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Belgium.
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Oct 14) 269 (41) 25255-8.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; AIDS
 ENTRY MONTH: 199411
 ENTRY DATE: Entered STN: 19941222
 Last Updated on STN: 19960129
 Entered Medline: 19941117

AB Determination of the three-dimensional structure of the human immunodeficiency virus type-1 (HIV-1) reverse transcriptase (RT) has indicated a totally different folding for the 51-kDa subunit (p51) than for the 66-kDa subunit (p66). The polymerase catalytic site is located on the p66 subunit. Moreover, the HIV-1-specific RT inhibitors, also designated as the non-nucleoside RT inhibitors (NNRTIs), select for amino acid mutations that afford resistance to these compounds and are clustered in the palm domain of the HIV-1 RT p66 subunit. This pocket is located in the vicinity of, but clearly distinct from, the polymerase active site. However, for the NNRTIs that belong to the class of the [2',5'-bis-O-(tert-butyldimethylsilyl)-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide)] (TSAO) derivatives, the resistance mutation is located at position Glu138. On the p66 subunit, this amino acid is distant from the binding site of the HIV-1-specific RT inhibitors. When the TSAO-specific resistance mutation Glu138-->Lys was introduced solely in the p51 subunit of the RT p66/p51 heterodimer, the enzyme proved completely resistant to TSAO-m3T but retained full sensitivity to TIBO R82150 and ddGTP. On the other hand, when the mutation was introduced only in the p66 subunit the enzyme remained equally sensitive to the inhibitory effects of TSAO-m3T, TIBO R82150, and ddGTP. Our data provide compelling evidence for a structural and functional role of the p51 subunit in the sensitivity and/or resistance of the enzyme to the NNRTIs.

L10 ANSWER 10 OF 14 MEDLINE on STN DUPLICATE 4
 ACCESSION NUMBER: 95110045 MEDLINE
 DOCUMENT NUMBER: 95110045 PubMed ID: 7529011
 TITLE: Subunit specificity of mutations that confer resistance to nonnucleoside inhibitors in human immunodeficiency virus type 1 reverse transcriptase.

AUTHOR: Boyer P L; Ding J; Arnold E; Hughes S H
CORPORATE SOURCE: ABL-Basic Research Program, NCI-Frederick Cancer Research and Development Center, Maryland 21702-1201.
CONTRACT NUMBER: NO1-CO-74101 (NCI)
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1994 Sep) 38 (9) 1909-14.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950215
Last Updated on STN: 19960129
Entered Medline: 19950127

AB We constructed plasmid vectors that simultaneously express both the p66 and p51 subunits of human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT) in Escherichia coli. These vectors allow us to generate HIV-1 RT heterodimers in which either the p66 or the p51 subunit has the wild-type sequence and the other subunit has a specific amino acid substitution. We used these vectors to express HIV-1 RT heterodimers containing several different amino acid substitutions reported to confer resistance to nonnucleoside inhibitors. Most of the amino acid substitutions conferred resistance to nonnucleoside inhibitors R86183 (TIBO) and TSAO-m3T only when present in the p66 subunit of the p66-p51 heterodimer; heterodimers that contained a wild-type p66 subunit and a mutant p51 subunit remained sensitive to the inhibitors. However, there was one mutation, E138K, that conferred drug resistance when the mutation was present in the p51 subunit. The corresponding heterodimer with the E138K mutation in the p66 subunit and a wild-type p51 subunit remained sensitive to the inhibitors. Analysis of the three-dimensional structure of HIV-1 RT indicated that residue 138 of the p51 subunit is in the nonnucleoside inhibitor-binding pocket while residue 138 of the p66 subunit is not. The mutagenesis results, combined with structural data, support the idea that the nonnucleoside inhibitors exert their effects by binding to a hydrophobic pocket in the RT heterodimer and that mutations which give rise to drug resistance directly interfere with the interactions between the nonnucleoside inhibitors and HIV-1 RT.

L10 ANSWER 11 OF 14 MEDLINE on STN
ACCESSION NUMBER: 94296403 MEDLINE
DOCUMENT NUMBER: 94296403 PubMed ID: 7517668
TITLE: Sensitivity of (138 Glu-->Lys) mutated human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT) to HIV-1-specific RT inhibitors.
AUTHOR: Balzarini J; Kleim J P; Riess G; Camarasa M J; De Clercq E; Karlsson A
CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Belgium.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1994 Jun 30) 201 (3) 1305-12.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940815
Last Updated on STN: 19960129
Entered Medline: 19940801

AB Human immunodeficiency virus type 1 (HIV-1) recombinant reverse transcriptase (RT) containing lysine (Lys) instead of glutamic acid (Glu) at position 138 proved fully resistant to the inhibitory effect of TSAO derivatives, but retained marked sensitivity to all other HIV-1-specific inhibitors investigated. In contrast, 181 Tyr-->Cys mutated RT lost sensitivity to all HIV-1-specific inhibitors. There was a close correlation between the sensitivity/resistance pattern of HIV-1-specific inhibitors against mutated (138 Glu-->Lys) recombinant HIV-1 RT and mutant virus strains selected for resistance against TSAO-m3T in cell culture and proven to contain the 138-Lys mutation as the sole mutation within the amino acid 50-270 region of their RT.

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on STN

ACCESSION NUMBER: 93241382 EMBASE

DOCUMENT NUMBER: 1993241382

TITLE: Treatment of human immunodeficiency virus type 1 (HIV-1)-infected cells with combinations of HIV-1-specific inhibitors results in a different resistance pattern than does treatment with single-drug therapy.

AUTHOR: Balzarini J.; Karlsson A.; Perez-Perez M.-J.; Camarasa M.-J.; Tarpley W.G.; De Clercq E.

CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium

SOURCE: Journal of Virology, (1993) 67/9 (5353-5359).

ISSN: 0022-538X CODEN: JOVIAM

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Human immunodeficiency virus type 1 (HIV-1)-infected CEM cells were treated by the HIV-1-specific inhibitors bis-heteroarylpiperazine (BHAP), 4,5,6,7-tetrahydro-5-methylimidazo[4,5,1-jk][1,4]benzodiazepin-2(1H)-one (TIBO) R82913, nevirapine, and the N3-methylthymine derivative of [2',5'-bis-O-(tert-butyldimethylsilyl)-β-D-ribofuranosyl]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide) (TSAO-m3T), as single agents or in combination, at escalating concentrations. When used individually, the compounds led to the emergence of drug-resistant virus strains within two to five subcultivations. The resulting strains were designated HIV-1/BHAP, HIV-1/TIBO, HIV-1/Nev, and HIV-1/TSAO-m3T, respectively. The mutant viruses showed the following amino acid substitutions in their reverse transcriptase (RT): Leu-100→Ile for HIV-1/BHAP; Lys-103→Asn for HIV-1/TIBO; Val-106→Ala for HIV-1/Nev; and Glu-138→Lys for HIV-1/TSAO-m3T. Both the Tyr-181→Cys and Val-106→Ala mutations were found in another mutant emerging following treatment with nevirapine at escalating concentrations. The BHAP-resistant virus remained fully sensitive to the inhibitory effects of nevirapine and TSAO-m3T, whereas the TSAO-m3T-resistant virus remained fully sensitive to the inhibitory effects of nevirapine and BHAP. When different pairs of nonnucleoside RT inhibitors (i.e., BHAP plus TSAO-m3T, nevirapine plus TSAO-m3T, TIBO plus TSAO-m3T, nevirapine plus TIBO, and BHAP plus nevirapine) were used, resistant virus emerged as fast as with single-drug therapy. In all cases the Tyr-181→Cys mutation appeared; the virus showed markedly reduced sensitivity to all HIV-1-specific inhibitors but retained sensitivity to 2',3'-dideoxynucleoside analogs such as zidovudine, ddC, and ddI. Our findings

argue against simultaneous combination of two different nonnucleoside RT inhibitors that are unable to inhibit HIV-1 mutant strains containing the Tyr-181→Cys mutation when administered as single drugs.

L10 ANSWER 13 OF 14 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 93349332 MEDLINE
DOCUMENT NUMBER: 93349332 PubMed ID: 8102234
TITLE: Metabolism and **pharmacokinetics** of the anti-HIV-1-specific inhibitor [1-[2',5'-bis-O-(tert-butyl-dimethylsilyl)-beta-D-ribofuranosyl]-3-N-methyl-thymine]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide).
AUTHOR: Balzarini J; Naesens L; Bohman C; Perez-Perez M J; San-Felix A; Camarasa M J; De Clercq E
CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Belgium.
SOURCE: BIOCHEMICAL PHARMACOLOGY, (1993 Jul 6) 46 (1) 69-77. Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19930924
Last Updated on STN: 19970203
Entered Medline: 19930907

AB [1-[2',5'-Bis-O-(tert-butyl-dimethylsilyl)-beta-D-ribofuranosyl]-3-N-methyl-thymine]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide) (TSAO-m3T) is a potent, selective and specific inhibitor of human immunodeficiency virus type 1 replication in vitro. Uptake of TSAO-m3T by human CEM cells is drug concentration-dependent and increased proportionally with increasing initial extracellular TSAO-m3T concentrations up to 20 micrograms/mL. Within 6 hr of incubation, the cells were almost completely saturated with the test compound; further incubation up to 72 hr did not markedly increase the intracellular concentration of the compound. No intracellular metabolic conversion of TSAO-m3T was observed in CEM, MT-4 or MOLT-4 cells. Upon intravenous bolus administration of TSAO-m3T to mice at 0.75 mg/kg, TSAO-m3T was rapidly cleared from the plasma in a mono-exponential manner (half-life: 22 min; distribution volume: 9.5 L/kg; total body clearance: 17.8 L/hr/kg). TSAO-m3T mainly accumulated in the lungs, followed by the heart, kidney and liver. Significant amounts of different metabolites of TSAO-m3T were detected in most tissues, the liver, kidney and spleen being the organs that showed the most extensive metabolism. The principal metabolites identified were TSAO-m3T derivatives in which the t-butyl-dimethylsilyl moiety at C-2' and/or C-5' had been split off. The free base N3-methylthymine was not detected.

L10 ANSWER 14 OF 14 MEDLINE on STN
ACCESSION NUMBER: 89388209 MEDLINE
DOCUMENT NUMBER: 89388209 PubMed ID: 2781261
TITLE: The piscine bioconcentration characteristics of cyclic and linear oligomeric permethylsiloxanes.
AUTHOR: Annelin R B; Frye C L
CORPORATE SOURCE: Health and Environmental Sciences, Dow Corning Corporation, Midland, MI 48686-0994.
SOURCE: SCIENCE OF THE TOTAL ENVIRONMENT, (1989 Jul 1) 83 (1-2) 1-11.

Journal code: 0330500. ISSN: 0048-9697.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891017

AB Using a conventional "resaturation" method whereby aquarium water was continuously passed through a column containing sand or fine glass beads coated with cyclic and linear permethylsiloxanes, their uptake levels by rainbow trout and fathead minnows have been compared. Because of the uncertainty associated with defining the actual aqueous concentrations of such poorly soluble substances, this study was focused on defining the "attainable uptake" levels from saturated solutions rather than precise definition of actual bioconcentration factor values. Although cyclic Me₂SiO-oligomers accumulated to a greater extent in fish than did comparable linear oligomers, uptake decreased sharply with increasing molecular weight. Thus, in the cyclic series (Dx), order of magnitude decreases were observed for each incremental molecular weight increase; i.e., for the compounds D4, D5, and D6 uptake levels of approximately 200, 20 and 2 ppm, respectively, were observed. Uptake of D8 was below our detection limit of 300 ppb. In the linear series, uptake of the tetramer MD2M was an order of magnitude less than observed for D4 and little or no uptake (i.e., less than 0.5 ppm) was observed for MD3M, MD4M and MD7M. The branched oligomer **M3T** exhibited levels comparable to its unbranched isomer MD2M, while M4Q was more comparable to the D6 uptake of 1-2 ppm. Very similar uptake levels of D5 resulted with and without a surfactant, even though the surfactant afforded a 20-fold increase in the D5 content of the water. This suggests that bio-availability is defined by the amount present in true solution as individual molecules and is not affected by the presence of aggregates or micelles. The highly inverse relationship observed in this study between uptake and molecular weight is strongly supportive of earlier estimates of a limiting molecular weight of about 600. These findings also strongly contradict a recent Japanese study, which concluded that bioconcentration not only occurred but actually increased with molecular weight in a series of commercial polydimethylsiloxane fluids. Also contrary to a recently published inference of biotransformation in fish, no evidence for such phenomena was observed in this study.

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L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:167776 HCAPLUS
DOCUMENT NUMBER: 134:212507
TITLE: Cosmetics containing branched volatile organopolysiloxanes
INVENTOR(S): Kuroda, Akihiro; Sakuta, Koji; Usui, Hitoshi
PATENT ASSIGNEE(S): Kanebo, Ltd., Japan; Shin-Etsu Chemical Co., Ltd.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015658	A1	20010308	WO 2000-JP5838	20000829
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1213006	A1	20020612	EP 2000-955104	20000829
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
PRIORITY APPLN. INFO.:			JP 1999-242948	A 19990830
			JP 1999-242949	A 19990830
			JP 1999-266824	A 19990921
			WO 2000-JP5838	W 20000829

AB Cosmetics characterized by containing an organopolysiloxane (Me₃SiO)₃SiMe (I). The cosmetics exhibit excellent volatility and feels and are excellent in stability. A compound I was prepared by hydrolysis of a mixture of trimethylchlorosilane and Me trichlorosilane, and combined at 25 % with silicone-treated TiO₂ particles 3, polyoxyethylene-methylpolysiloxane copolymer (KF6017) 1, silicone-treated zinc oxide particle 6, perfluoroalkylphosphate-treated mica 0.5, crosslinked organopolysiloxane spherical powders 4, dimethylpolysiloxane (KF96A-6) 2, fluorinated dimethiconol 1, trimethylsiloxysilicate solution 6, octyl-p-methoxysilicate 3, p-fluoropolyether 0.5, ethanol 10, ale extract 1, hamamelis extract 1, hibiscus extract 0.5, and water q.s. to 100 % to obtain a sunscreen makeup base.

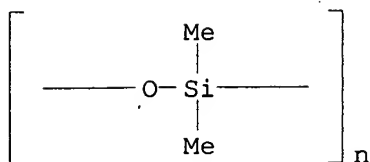
IT 9016-00-6, KF 96A100

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

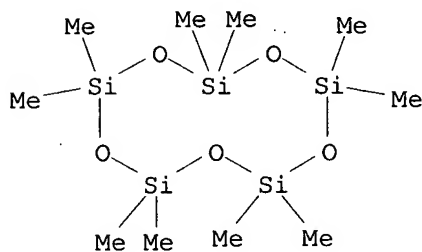
(KF 96A6, KF 96A100; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)

RN 9016-00-6 HCAPLUS

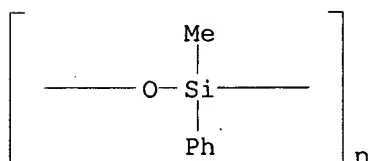
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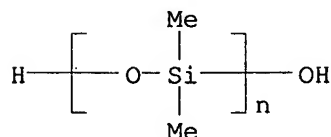
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 derivs. 257905-55-8, KF7312J 314020-17-2, KSG15
 319427-75-3, KF 6026
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (cosmetics containing branched volatile organopolysiloxanes and other
 polysiloxanes)
 RN 541-02-6 HCAPLUS
 CN Cyclopentasiloxane, decamethyl- (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 9005-12-3 HCAPLUS
 CN Poly[oxy(methylphenylsilylene)] (8CI, 9CI) (CA INDEX NAME)



RN 31692-79-2 HCAPLUS
 CN Poly[oxy(dimethylsilylene)], α -hydro- ω -hydroxy- (8CI, 9CI)
 (CA INDEX NAME)



RN 56275-01-5 HCAPLUS
 CN Silicic acid, trimethylsilyl ester (9CI) (CA INDEX NAME)

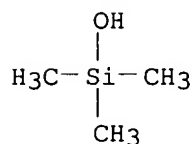
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CRN 1343-98-2
CMF Unspecified
CCI MAN

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CM 2

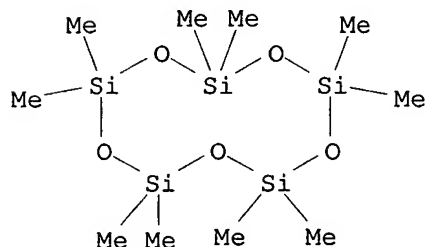
CRN 1066-40-6
CMF C3 H10 O Si



RN 257905-55-8 HCAPLUS
CN Silicic acid, trimethylsilyl ester, mixt. with
decamethylcyclopentasiloxane (9CI) (CA INDEX NAME)

CM 1

CRN 541-02-6
CMF C10 H30 O5 Si5



CM 2

CRN 56275-01-5
CMF C3 H10 O Si . x Unspecified

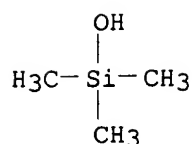
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CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

CRN 1066-40-6
CMF C3 H10 O Si



RN 314020-17-2 HCAPLUS
CN KSG 15 (9CI) (CA INDEX NAME)

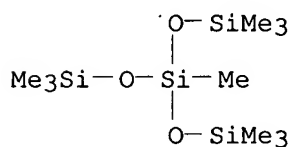
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RN 319427-75-3 HCAPLUS
CN Oleyldimethicone copolyol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

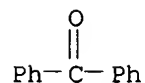
IT 17928-28-8P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)

RN 17928-28-8 HCAPLUS
CN Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]- (9CI) (CA INDEX NAME)



IT 119-61-9D, Benzophenone, derivs. 1314-13-2, Zinc oxide, biological studies 5466-77-3, 2-Ethylhexyl-p-Methoxycinnamate 13463-67-7, Titanium oxide, biological studies 70356-09-1, Butyl methoxydibenzoylmethane
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes and sunscreen agents)

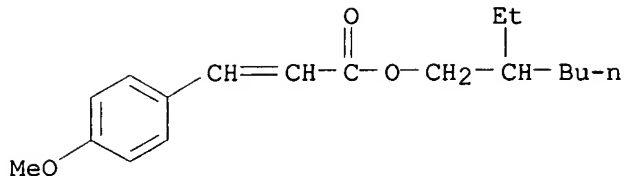
RN 119-61-9 HCAPLUS
CN Methanone, diphenyl- (9CI) (CA INDEX NAME)



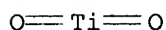
RN 1314-13-2 HCAPLUS
CN Zinc oxide (ZnO) (9CI) (CA INDEX NAME)



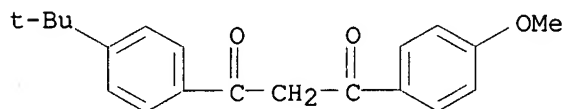
RN 5466-77-3 HCAPLUS
CN 2-Propenoic acid, 3-(4-methoxyphenyl)-, 2-ethylhexyl ester (9CI) (CA INDEX NAME)



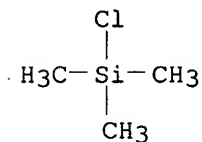
RN 13463-67-7 HCAPLUS
 CN Titanium oxide (TiO₂) (8CI, 9CI) (CA INDEX NAME)



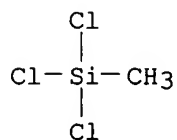
RN 70356-09-1 HCAPLUS
 CN 1,3-Propanedione, 1-[4-(1,1-dimethylethyl)phenyl]-3-(4-methoxyphenyl)-
 (9CI) (CA INDEX NAME)



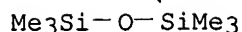
IT 75-77-4, Trimethylchlorosilane, reactions 75-79-6,
 Methyltrichlorosilane 107-46-0, Hexamethyldisiloxane
 1185-55-3, Methyltrimethoxysilane
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of branched volatile organopolysiloxanes for cosmetics)
 RN 75-77-4 HCAPLUS
 CN Silane, chlorotrimethyl- (8CI, 9CI) (CA INDEX NAME)



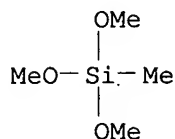
RN 75-79-6 HCAPLUS
 CN Silane, trichloromethyl- (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 107-46-0 HCAPLUS
 CN Disiloxane, hexamethyl- (8CI, 9CI) (CA INDEX NAME)



RN 1185-55-3 HCAPLUS
 CN Silane, trimethoxymethyl- (6CI, 8CI, 9CI) (CA INDEX NAME)



IC ICM A61K007-00
 CC 62-4 (Essential Oils and Cosmetics)
 ST cosmetic volatile siloxane organopolysiloxane
 IT Silicone rubber, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (KSG 21; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
 IT Fluoropolymers, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (Me trifluoropropyl polysiloxane-, polyoxyethylene-, FPD 6131; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
 IT Polysiloxanes, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (Me trifluoropropyl, polyoxyethylene-, FPD 6131; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
 IT Silsesquioxanes
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (Me, KMP 590; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
 IT Polysiloxanes, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (acrylic, KP 561, KP 562; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
 IT Shaving preparations
 (aftershave; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
 IT Silsesquioxanes
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (alkyl, spherical; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
 IT Polysiloxanes, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (amino; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
 IT Antiperspirants
 Deodorants
 Sunscreens

- Suntanning agents
(cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
Hair preparations
(creams; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(cyclosiloxane-, di-Me; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Silicone rubber, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(di-Me, KMP 594; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(di-Me, Me Ph, KF 56; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(di-Me, Me hydrogen, KSG 16; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(di-Me, hydroxyalkyl Me, ethoxylated, KF 6017; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(di-Me, polyoxyethylene-polyoxypropylene-, KF 6012; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(di-Me, polyoxyethylene-polyoxypropylene-, graft, KF 615A; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
(emulsions; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
(eye liners; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
(eye shadows; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(fluorine-containing, FL 100; cosmetics containing branched volatile

- organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
(foundations; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
(gels; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
(hand creams; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(hydroxy; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
(lotions; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cosmetics
(mascaras; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(methacrylate-, KP 545; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(polyether-; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polysiloxanes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(polyoxyalkylene-, KF 6015; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Fluoropolymers, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(polysiloxane-, FL 100; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(polysiloxane-, KF 6015; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Cyclosiloxanes
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(siloxane-, di-Me; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT Polyethers, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(siloxane-; cosmetics containing branched volatile organopolysiloxanes and other polysiloxanes)
- IT 9016-00-6, KF 96A100
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(KF 96A6, KF 96A100; cosmetics containing branched volatile

- organopolysiloxanes and other polysiloxanes)
- IT 541-02-6, KF 995 9005-12-3, Methylphenylpolysiloxane
31692-79-2D, Dimethiconol, fluorinated 56275-01-5D,
derivs. 257905-55-8, KF7312J 314020-17-2, KSG15
319427-75-3, KF 6026
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(cosmetics containing branched volatile organopolysiloxanes and other
polysiloxanes)
- IT 17928-28-8P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); USES (Uses)
(cosmetics containing branched volatile organopolysiloxanes and other
polysiloxanes)
- IT 119-61-9D, Benzophenone, derivs. 1314-13-2, Zinc oxide,
biological studies 5466-77-3, 2-Ethylhexyl-p-Methoxycinnamate
13463-67-7, Titanium oxide, biological studies 70356-09-1
, Butyl methoxydibenzoylmethane
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(cosmetics containing branched volatile organopolysiloxanes and other
polysiloxanes and sunscreen agents)
- IT 75-77-4, Trimethylchlorosilane, reactions 75-79-6,
Methyltrichlorosilane 107-46-0, Hexamethyldisiloxane
1185-55-3, Methyltrimethoxysilane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of branched volatile organopolysiloxanes for cosmetics)
- REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his ful

FILE 'HCAPLUS' ENTERED AT 14:34:43 ON 30 NOV 2003

E KURODA AKIHIRO/AU
 L1 296 SEA ABB=ON "KURODA AKIHIRO"/AU
 E SAKUTA KOJI/AU
 L2 62 SEA ABB=ON "SAKUTA KOJI"/AU
 E USUI HITOSHI/AU
 L3 3 SEA ABB=ON "USUI HITOSHI"/AU
 L4 1 SEA ABB=ON L1 AND L2 AND L3

*Inventor
search*

FILE 'REGISTRY' ENTERED AT 14:37:47 ON 30 NOV 2003

L5 18 SEA ABB=ON (107-46-0/BI OR 1185-55-3/BI OR 119-61-9/BI OR
 1314-13-2/BI OR 13463-67-7/BI OR 17928-28-8/BI OR 257905-55-8/B
 I OR 314020-17-2/BI OR 31692-79-2/BI OR 319427-75-3/BI OR
 541-02-6/BI OR 5466-77-3/BI OR 56275-01-5/BI OR 70356-09-1/BI
 OR 75-77-4/BI OR 75-79-6/BI OR 9005-12-3/BI OR 9016-00-6/BI)

FILE 'HCAPLUS' ENTERED AT 14:38:13 ON 30 NOV 2003

L6 1 SEA ABB=ON L4 AND L5

FILE 'REGISTRY' ENTERED AT 14:41:37 ON 30 NOV 2003

L7 1 SEA ABB=ON (17928-28-8/RN)

*RN of compound requested - display of
compound is attached.*

FILE 'HCAPLUS' ENTERED AT 14:42:13 ON 30 NOV 2003

L8 5 SEA ABB=ON (L7 OR M3T) AND (?DERM? ?SKIN? OR ?CUTAN? OR
 ?PHARM? OR ?COSMET? OR ?PERSON?(W)?CARE?)

5 hits in CAPLUS

FILE 'MEDLINE, BIOSIS, EMBASE, JICST-EPLUS, JAPIO, RAPRA, KOSMET,
 PLASPEC' ENTERED AT 14:44:48 ON 30 NOV 2003

L9 19 SEA ABB=ON L8

L10 14 DUP REMOV L9 (5 DUPLICATES REMOVED)

14 hits in other d.b.'s

*If you would like this search broadened to
 "organosiloxanes", please let me know - it won't take long.*

*Thank you,
 Mary Jane Ruhl
 605-1155*

Set Name Query

side by side

Hit Count Set Name

result set

*DB=USPT; PLUR=YES; OP=OR*L17 L16 and (crosslinked cross-linked) and fluorin\$.ab.9 L17*DB=USPT,PGPB; PLUR=YES; OP=OR*L16 (fluorin\$ and organopolysiloxane) and (methylphenylpolysiloxane cyclomethicone methylpolysiloxane octamethylcyclo\$ (low-viscosity) (low adj viscosity adj oil))426 L16*DB=USPT; PLUR=YES; OP=OR*L15 L1417 L15*DB=USPT,PGPB; PLUR=YES; OP=OR*L14 L13 and cross\$21 L14*DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR*L13 (fluorin\$ near10 organopolysiloxane) and (methylphenylpolysiloxane cyclomethicone methylpolysiloxane octamethylcyclo\$ (low-viscosity) (low adj viscosity adj oil))44 L13*DB=USPT; PLUR=YES; OP=OR*L12 (fluorin\$ near10 organopolysiloxane near10 cross\$) and (methylphenylpolysiloxane cyclomethicone methylpolysiloxane octamethylcyclo\$ (low-viscosity) (low adj viscosity adj oil))0 L12L11 (fluorin\$ and organopolysiloxane and cross\$) and (methylphenylpolysiloxane cyclomethicone methylpolysiloxane octamethylcyclo\$ (low-viscosity) (low adj viscosity adj oil))236 L11L10 L8 and (methylphenylpolysiloxane cyclomethicone methylpolysiloxane octamethylcyclo\$ (low-viscosity) (low adj viscosity adj oil))0 L10L9 L8 and (methylphenylpolysiloxane (low-viscosity) (low adj viscosity adj oil))0 L9L8 (fluorin\$ and organopolysiloxane and cross\$).ab.5 L8L7 (fluor\$ near20 organopolysiloxane near20 cross\$)17 L7L6 (flour\$ near20 organopolysiloxane near20 cross\$)0 L6L5 (flour\$ and organopolysiloxane and cross\$).ab.0 L5L4 L3 and volati\$0 L4L3 6395857.pn. and (paste solid liquid)1 L3L2 L1 and dimethylpolysiloxane0 L2L1 6395857.pn. and gum0 L1

END OF SEARCH HISTORY